Food and Drug Administration
Center for Drug Evaluation and Research

SUMMARY MINUTES
ENDOCRINOLOGIC AND METABOLIC DRUGS ADVISORY COMMITTEE #70

May 15, 1998
Bethesda Holiday Inn
8120 Wisconsin Avenue, Bethesda MD

Members Present
Robert Marcus, M.D., Acting Chair
Robert Sherwin, M.D.
D. Roger Illingworth, M.D., Ph.D.
Jules Hirsch, M.D.
Mark Molitch, M.D.
Maria I. New, M.D.
Jaime Davidson, M.D.
Cathy Critchlow, Ph.D.

FDA Participants
James M. Bilstad, M.D.
Solomon Sobel, M.D.
David Orloff, M.D.
Jean Temeck, M.D.
Sonia Castillo, Ph.D.

Consultants
Pippa Simpson, Ph.D.
Glenn Braunstein, M.D.
Kenneth Burman, M.D.
Vernon M. Chinchilli, Ph.D.

Guest Experts

Members Absent
Robert A. Kreisberg, M.D.
Jose Francisco Cara, M.D.
Henry G. Bone, III, M.D.

Executive Secretary
Kathleen R. Reedy

These summary minutes for the May 15, 1998 meeting of the Endocrinologic and Metabolic Drugs Advisory Committee were approved on 9/25/99.

I certify that I attended the May 15, 1998 meeting of the Endocrinologic and Metabolic Drugs Advisory Committee and that these minutes accurately reflect what transpired.

Kathleen R. Reedy,
Executive Secretary

Robert Marcus, M.D.
Acting Chairperson

The third day of the 70th meeting of the Endocrinologic and Metabolic Drugs Advisory Committee took place at the Bethesda Holiday Inn, 8120 Wisconsin Avenue, Bethesda, MD on May 15, 1998 and was attended by approximately 275 persons. The meeting was held to discuss the efficacy and safety of NDA 20-898, Thyrogen™ [thyrotropin alpha, rTSH] presented by Genzyme as an adjunct for the detection of thyroid cancer. The Committee had been provided a briefing document from the sponsor and the agency approximately twenty one days before the meeting.

The meeting was called to order, introductions of the participants and opening comments were made by Robert Marcus, M.D., Acting Chair of the Endocrinologic and Metabolic Drugs Advisory Committee. The meeting statement regarding conflict of interest of the participants was read by Kathleen Reedy, Executive Secretary of the Endocrinologic and Metabolic Drugs Advisory Committee.

There were three speakers at the Open Public Hearing in support of approval of the product.

1. Richard Robbins, MD, Chief, Endocrinology Service, Memorial Sloan-Kettering Cancer Center, Professor of Medicine, Cornell University
2. Maura Goldsborough, RN, patient
3. Melvin R. Smith, patient

Eighteen letters were presented at the open public hearing in favor of approval.

1. F. Deaver Thomas, M.D., Professor of Radiology and Medicine
   Director, Nuclear Medicine Division, University Hospital
   SUNY Health Science Center at Syracuse
2. Howard M. Lando, MD, Consultative Endocrinology, Reston, Alexandria, VA
3. Elias C. Dow, M.D.
4. Norman Fleischer, M.D., Professor of Medicine,
   Director of Medicine and the Diabetes Research Center
   Albert Einstein College of Medicine of Yeshiva University
5. Donald Margouleff, M.D., Chief, Division of Nuclear Medicine
   North Shore University Hospital, Manhasset, NY
6. Steven M. Larson, M.D., Chief, Nuclear Medicine Service, Department of Radiology, Memorial Sloan-Kettering Cancer Center; Director, Laurent and Alberta Gerschel PET Center, Professor of Radiology, Cornell University.
7. American Thyroid Association, Martin I. Surks, M.D., Secretary
8. American Association of Clinical Endocrinologists,
   Helena W. Rodbard, M.D., F.A.C.E., President
9. Richard S. Cherlin, M.D., Los Gatos, CA
10. Amiel Zachary Rudavsky, M.D., P.C., New York, NY
11. Sanford R. Mallin, M.D., Chairman, Clinical Initiatives Committee, Endocrine Society
12. The Thyroid Society for Education and Research,
    Steven I. Sherman, M.D., Medical Director

13. Amy L. O'Donnell, M.D., Chief, Division of Endocrinology and Metabolism
    VA Western New York Healthcre System
    Research Assistant Professor of Medicine, State University of New York at Buffalo
14. Robert F. Gagel, M.D., Chair, Department of Medical Specialties
    Chief, Section of Endocrinology, The University of Texas M. D. Anderson Cancer Center
    Texas Medical Center, Houston, TX
15. Leslie J. DeGroot, M.D., Professor of Medicine
    University of Chicago Medical Center, Thyroid Study Unit
16. M. Elizabeth Mason, M.D., The Diabetes Institute and
    Center for Endocrine and Metabolic Disorders, Norfolk, VA
17. Luis E. Tenorio, M.D., Chief, Nuclear Medicine Service
    James A. Haley Veterans' Hospital, Tampa, FL
18. Tonia Suchocki, patient

The Genzyme Presentation consisted of:

Introduction: A. Lawton, Vice President Regulatory Affairs
Current Management of Thyroid Cancer: E. Mazzaferri, M.D.
Clinical Safety and Efficacy: D. Meeker, M.D., Vice President, Medical Affairs
Clinical Settings for the Use of Thyrogen: E. Mazzaferri, M.D.
Summary: R. Moscicki, M.D., Chief Medical Officer

The FDA Presentation was:

Medical Review: Jean Temeck, M.D., Medical Officer
Division of Metabolic and Endocrine Drug Products
Statistical Review: Sonia Castillo, Ph.D.
Office of Epidemiology and Biostatistics, Division of Biometrics III
Overview: David Orloff, M.D., Medical Officer, Group Leader
Division of Metabolic and Endocrine Drug Products

For the discussion the following issues were addressed.

Advisory Committee advice and opinion is sought regarding:

1. The adequacy of the Thyrogen phase 3 studies to address the following issues:
   a. the overall (combining scan and thyroglobulin) utility of Thyrogen as an alternative diagnostic agent to withdrawal (WD) for guiding clinical decision-making in patients with a history of well-differentiated thyroid cancer.
   b. the diagnostic utility of Thyrogen thyroglobulin vs. Thyroglobulin (tg) on thyroid hormone suppressive therapy (THST) in the follow-up of low-risk patients with a history of well-differentiated thyroid cancer.
2. The acceptability of the Thyrogen scan false negative rate (in patients with evidence of disease by WD scanning) if Thyrogen were to be used as a general substitute for WD in follow up of patients with a history of well-differentiated thyroid cancer.
3. The use of a Thyrogen thyroglobulin level as an independent, reliable marker of both the presence of thyroid cancer and of the burden of tumor, and the utility of a Thyrogen tg level in guiding clinical management decisions in patients with thyroid cancer.

4. The place for Thyrogen testing in the follow-up of patients with well-differentiated thyroid cancer.

Members agreed that Thyrogen is a useful clinical tool and not a substitute for WD, would reduce the frequency of WD, and is better than anything else except WD. The Phase 3 studies were a post-hoc analysis. The protocol is not well tested. It is not 100% specific and sensitive, but is a very good alternative to WD. Further study is required with a standard of truth for validation. Meanwhile it is a clinically useful tool. As experienced clinicians would be reasonably informed and thyroid endocrinologists and nuclear medicine specialists would be using clinical judgement, it is a useful tool to integrate into their armamentarium, allowing them flexibility in modalities. Thyrogen use would prevent the misery of hypothyroidism and the postponment of scanning by patients of an essentially primitive withdrawal protocol. With further studies and devemopment, the protocol would change and improve.

The specific questions were answered as follows:

1. Taking into account the risks and benefits associated with its revised proposed use, should Thyrogen be approved for use in conducting thyroid scanning and thyroglobulin testing in the follow-up of patients with well differentiated thyroid cancer as a definitive substitute for withdrawal?
   No: 11 Yes: 0
2. Taking into account the risks and benefits associated with its revised proposed use, should Thyrogen be approved for use in conducting thyroid scanning and thyroglobulin testing in the follow-up of patients with well differentiated thyroid cancer who are either unable to mount an adequate endogenous TSH response after withdrawal or for whom withdrawal is medically contra-indicated?
   Yes: 12 No: 0
3. Taking into account the risks and benefits associated with its revised proposed use, should Thyrogen be approved for use in conducting thyroid scanning and thyroglobulin testing in the follow-up of patients with well differentiated thyroid cancer in place of thyroglobulin testing alone?
   Yes: 12 No: 0
4. Taking into account the risks and benefits associated with its revised proposed use, should Thyrogen be approved for use in conducting thyroid scanning and thyroglobulin testing in the follow-up of patients with well differentiated thyroid cancer as an adjunct or alternative to withdrawal?
   Yes: 8 No: 3

The meeting was adjourned at 2:00 pm.

Kathleen Reedy, Executive Secretary
Endocrinologic and Metabolic Drugs Advisory Committee